

(FILE 'HOME' ENTERED AT 11:32:29 ON 01 AUG 2000)

FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS, SCISEARCH' ENTERED AT 11:32:33 ON
01 AUG 2000

L1 29500 S REV
L2 1425 S L1 AND (VECTOR OR CONSTRUCT)
L3 257 S L2 AND RRE OR (REV BINDING SUBSEQUENCE)
L4 257 S L2 AND (RRE OR (REV BINDING SUBSEQUENCE))
L5 12 S L4 AND (SPLICE AND (DONOR OR ACCEPTOR))
L6 5 DUP REM L5 (7 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 11:36:59 ON 01 AUG 2000

FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS, SCISEARCH' ENTERED AT 11:40:24 ON
01 AUG 2000

L7 20 S REV (A) DEPENDENT (A) GENE (A) EXPRESSION
L8 6 DUP REM L7 (14 DUPLICATES REMOVED)
L9 1 S PBAR (A) EDN
L10 8 S EDN AND REV
L11 3 DUP REM L10 (5 DUPLICATES REMOVED)
L12 182 S REV AND RNASE
L13 0 S L12 AND ONCONASE
L14 0 S L12 AND SPLICE DONOR
L15 40 S L12 AND RRE
L16 19 DUP REM L15 (21 DUPLICATES REMOVED)

✓ 65 5958768

(FILE 'HOME' ENTERED AT 11:32:29 ON 01 AUG 2000)

FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS, SCISEARCH' ENTERED AT 11:32:33 ON
01 AUG 2000

L1	29500 S REV
L2	1425 S L1 AND (VECTOR OR CONSTRUCT)
L3	257 S L2 AND RRE OR (REV BINDING SUBSEQUENCE)
L4	257 S L2 AND (RRE OR (REV BINDING SUBSEQUENCE))
L5	12 S L4 AND (SPLICE AND (DONOR OR ACCEPTOR))

L6 ANSWER 1 OF 5 MEDLINE DUPLICATE 1
 ACCESSION NUMBER: 1999292922 MEDLINE
 DOCUMENT NUMBER: 99292922
 TITLE: Contributions of viral **splice** sites and
 cis-regulatory elements to lentivirus **vector**
 function.
 AUTHOR: Cui Y; Iwakuma T; Chang L J
 CORPORATE SOURCE: Department of Molecular Genetics and Microbiology, Gene
 Therapy Center, and University of Florida Brain Institute,
 College of Medicine, University of Florida, Gainesville,
 Florida 32610-0266, USA.
 CONTRACT NUMBER: HL-59412 (NHLBI)
 SOURCE: JOURNAL OF VIROLOGY, (1999 Jul) 73 (7) 6171-6.
 Journal code: KCV. ISSN: 0022-538X.
 PUB. COUNTRY: United States
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals; Cancer Journals
 ENTRY MONTH: 199909
 ENTRY WEEK: 19990905

AB The mobile transgene constructs of most human immunodeficiency virus
 (HIV)-based lentivirus vectors currently in use contain viral long
 terminal repeats, a 5' untranslated region, gag sequences, and env
 sequences that include the **Rev**-responsive element (**RRE**
). In this study, we examined the possibility of deleting HIV
splice sites and gag and env sequences from an HIV type 1
 recombinant **vector** established in our laboratory as part of our
 ongoing efforts to improve this **vector** system. Mutations in the
 major **splice donor** site (SD) markedly reduced viral
 RNA expression but had little effect on **vector** titer. Deletion
 of gag or env sequences, excluding **RRE**, led to a moderate
 reduction in **vector** titer. Interestingly, deletion of
RRE slightly reduced viral RNA expression but markedly impaired
vector function. Combined deletions of **RRE**, gag (except
 for the first 40 nucleotides), env, and the SD mutation resulted in a
 twofold increase in cytoplasmic viral RNA expression and a recovery of
vector efficiency to approximately 50% of the wild-type level.
 This increase in cytoplasmic RNA levels is likely to be due, at least in
 part, to effects of the TE671 host cells, a human rhabdomyosarcoma cell
 line used for **vector** production in our system, on the
 cytoplasmic distribution of spliced and unspliced viral RNA. These
 results
 show that optimal lentivirus **vector** function can be maintained
 in the absence of multiple essential viral elements.

L6 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2000 ACS
 ACCESSION NUMBER: 1998:268635 CAPLUS
 DOCUMENT NUMBER: 128:291139
 TITLE: Construction of TRIN retroviral vectors contg.
Rev-responsive element of HIV1 virus
 INVENTOR(S): Kingsman, Susan Mary; Kingsman, Alan John
 PATENT ASSIGNEE(S): Oxford Biomedica (UK) Ltd., UK; Kingsman, Susan Mary;
 Kingsman, Alan John
 SOURCE: PCT Int. Appl., 38 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9817817	A1	19980430	WO 1997-GB2859	19971017
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9747124	A1	19980515	AU 1997-47124	19971017
GB 2331989	A1	19990609	GB 1999-4143	19971017
EP 931157	A1	19990728	EP 1997-909438	19971017
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.:			GB 1996-21679	19961017
			WO 1997-GB2859	19971017
AB Retroviral vector particles having an RNA genome carrying sequences which provide in the DNA provirus at least one selected gene located within an intron in a transcription unit of the provirus, which transcription unit further comprises a polynucleotide response element which is responsive to a nucleus to cytoplasm transport factor such as HIV				
Rev. These vectors have been named TRIN (Tat and Rev inducible) vectors. Expression of the selected genes is thus rendered Rev-dependent and so is dependent upon the presence of HIV. The TRIN vectors also contain the murine leukemia virus splice donor site, the strong CMV promoter, a packaging signal, and the HIV U5 and R regions.				
L6 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2000 ACS				
ACCESSION NUMBER:		1998:89371 CAPLUS		
DOCUMENT NUMBER:		128:150403		
TITLE:		Construction of retroviral vectors for delivering viral and oncogenic inhibitors		
INVENTOR(S):		Raybak, Susanna M.; Cara, Andrea; Gusella, Gabriele Luca; Newton, Dianne L.		
PATENT ASSIGNEE(S):		United States Dept. of Health and Human Services, USA;		
		Raybak, Susanna M.; Cara, Andrea; Gusella, Gabriele Luca; Newton, Dianne L.		
SOURCE:		PCT Int. Appl., 63 pp. CODEN: PIXXD2		
DOCUMENT TYPE:		Patent		
LANGUAGE:		English		
FAMILY ACC. NUM. COUNT:		1		
PATENT INFORMATION:				

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9803669	A2	19980129	WO 1997-US12637	19970717
WO 9803669	A3	19980226		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9738049	A1	19980210	AU 1997-38049	19970717
EP 917585	A2	19990526	EP 1997-935014	19970717

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI

PRIORITY APPLN. INFO.:

US 1996-22052 19960722

WO 1997-US12637 19970717

AB Cell transformation vectors for inhibiting HIV and tumor growth are provided. Optionally, the vectors encode RNases A superfamily members such as eosinophil-derived neurotoxin (EDN) and onconase. Cells transduced by the vectors and methods of transforming cells (in vitro and in vivo) using the vectors are also provided. The viral and oncogene inhibitors are typically linked to a promoter such as retroviral HIV LTR promoters, the CMV promoter, the probasin promoter, and tetracycline-responsive promoters. The method is exemplified by construction of a viral **vector** contg. a HIV **Rev**-responsive element, an encephalomyocarditis virus internal ribosome entry site, a first viral inhibitor subsequence (for immunodominant proteins such as as Tat, Gag, or **Rev**), **splice donor** site subsequence, **splice acceptor** site subsequence, the above mentioned promoter, and the EDN coding sequence. The **vector** may be packaged in a liposome and its contents transduced into CD34+ hematopoietic stem cells, CD4+ cells, and transferrin receptor+ cells. Claimed vectors include pBAR, pBAR-ONC, and pBAR-EDN.

L6 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1994:673849 CAPLUS

DOCUMENT NUMBER: 121:273849

TITLE: Manufacture of antigens in gag protein-based particles

using a minimal retroviral expression cassette

INVENTOR(S): Czaplewski, Lloyd George

PATENT ASSIGNEE(S): British Bio-Technology Ltd., UK

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
✓ WO 9420621	A2	19940915	WO 1994-GB281	19940211
WO 9420621	A3	19941013		
W:	AU, CA, CN, DE, FI, GB, JP, KR, NO, NZ, RU, UA, US			
RW:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE			
AU 9460063	A1	19940926	AU 1994-60063	19940211
PRIORITY APPLN. INFO.:			GB 1993-4239	19930301
			WO 1994-GB281	19940211

AB An expression cassette using a single promoter to drive expression of a gag-derived sequence from a complex retrovirus including a **rev** gene, an **RRE** element and **donor** and **acceptor** elements is described for use in the manuf. of retroviral particles presenting antigens for use in vaccines. The **construct** is arranged to ensure that the promoter is capable of driving expression of both the gag-derived sequence and the **rev**-like element. The **construct** does not contain a functional env gene. The construction of a series of such cassettes for the synthesis of tat protein is demonstrated. COS-7 cells co-transfected with one of these constructs and a CAT gene under control of a tat-responsive promoter showed high levels of expression of the CAT gene.

L6 ANSWER 5 OF 5 MEDLINE

DUPLICATE 2

ACCESSION NUMBER: 90045468 MEDLINE

DOCUMENT NUMBER: 90045468

TITLE: HTLV-1 rex and HIV-1 **rev** act through similar mechanisms to relieve suppression of unspliced RNA

expression.
AUTHOR: Itoh M; Inoue J; Toyoshima H; Akizawa T; Higashi M;
Yoshida
CORPORATE SOURCE: M
Department of Viral Oncology, Cancer Institute, Tokyo,
Japan.
SOURCE: ONCOGENE, (1989 Nov) 4 (11) 1275-9. *Not in*
Journal code: ONC. ISSN: 0950-9232.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199002
AB Human retroviruses, human T cell leukemia viruses (HTLV) and human immunodeficiency viruses (HIV), express two classes of mRNAs; fully spliced mRNA in the early phase and intron-containing mRNA in a later phase. The expressions of HTLV-1 rex and HIV **rev** by early mRNAs are essential for the later phase of expression of intron-containing gag and env mRNAs. Each two cis-acting sequences seem to be involved in these regulations: HTLV-1 rex depends on a **splice donor** (SD) and a responsible element (RXE) at the 3' end, whereas HIV **rev** depends on a specific repressive sequence (CRS) and a responsible element (**RRE**) in the intron, but does not require an SD. For analyses of these cis-acting sequences, we inserted an HIV element **RRE** into an HTLV-1 **construct** and tested the responses to HTLV-1 rex and HIV **rev** regulations. The results indicated that both rex and **rev** could regulate RNA expression of these chimeric constructs responding to an HIV **RRE**. A repressive element (CRS) was dispensable, and the intronic or exonic location of **RRE** was not important. These observations suggest that rex and **rev** could be functionally equivalent to induce cytoplasmic expression of unspliced RNA which expression is suppressed either by an SD or CRS depending on the construction.

ANSWER 3 OF 3 MEDLINE

DUPLICATE 2

ACCESSION NUMBER: 1998197329

MEDLINE

DOCUMENT NUMBER: 98197329

TITLE: Inhibition of HIV-1 replication by combined expression of gag dominant negative mutant and a human ribonuclease in a tightly controlled HIV-1 inducible vector.

AUTHOR: Cara A; Rybak S M; Newton D L; Crowley R; Rottschaefer S E; Reitz M S Jr; Gusella G L

CORPORATE SOURCE: Basic Research Laboratory, NCI, NIH, Bethesda, MD, USA.

SOURCE: GENE THERAPY, (1998 Jan) 5 (1) 65-75.

Journal code: CCE. ISSN: 0969-7128.

PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199806

ENTRY WEEK: 19980603

AB An HIV-1-based expression vector has been constructed that produces protective genes tightly regulated by HIV-1 Tat and **Rev** proteins. The vector contains either a single protective gene (HIV-1 gag dominant negative mutant (delta-gag)) or a combination of two different protective genes (delta-gag and eosinophil-derived neurotoxin (**EDN**), a human ribonuclease) which are expressed from a dicistronic mRNA. After stable transfection of CEM T cells and following challenge with HIV-1, viral production was completely inhibited in cells transduced with the vector producing both delta-gag and **EDN** and delayed in cells producing delta-gag alone. In addition, cotransfection of HeLa-Tat cells with an infectious HIV-1 molecular clone and either protective vector demonstrated that the HIV-1 packaging signals present in the constructs were functional and allowed the efficient assembly of the protective RNAs into HIV-1 virions, thus potentially transmitting protection to the HIV-1 target cells.

Applent 3

RB155.8.

G-462